

STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 156375

TO: Rei-Tsang Shiao
Location: 5a10 / 5c18
Tuesday, June 28, 2005
Art Unit: 1626
Phone: 571-272-0707
Serial Number: 09 / 653563

From: Jan Delaval
Location: Biotech-Chem Library
Remsen 1a51
Phone: 571-272-2504
jan.delaval@uspto.gov

Search Notes

Jan Delavan
for search

Access DB#

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Robert (Bob) Shiao Examiner #: 79521 Date: 6/15/05
Alt Unit: 1626 Phone Number: 2-0907 Serial Number: 091653, 56
Mail Box and Bldg Room Location: 5A10/3C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

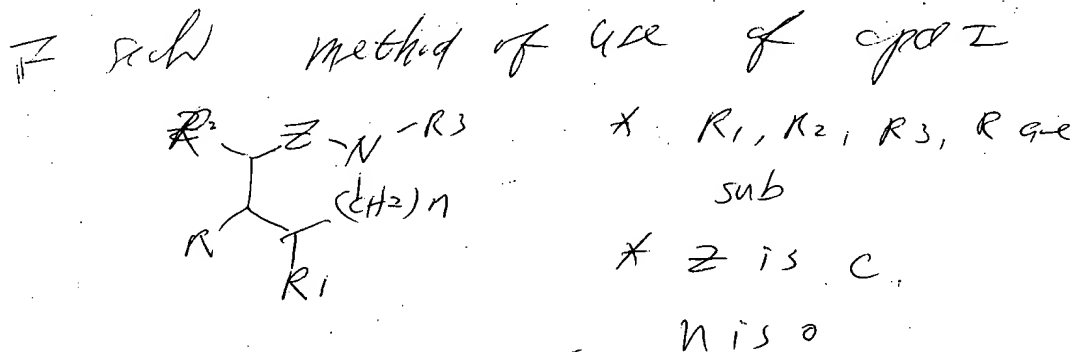
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Yoon et al

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



II. sch method of use of
compounds in claims 170-171, 175-176,
and 190-191

STAFF USE ONLY

Searcher: an
Searcher Phone #: 22504
Searcher Location: _____
Date Searcher Picked Up: 6/28/05
Date Completed: 6/28/05
Searcher Prep & Review Time: _____
Technical Prep Time: 20
Online Time: +35

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) ☒ _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN ☒ _____
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

=> fil reg

FILE 'REGISTRY' ENTERED AT 15:44:05 ON 28 JUN 2005
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
 provided by InfoChem.

STRUCTURE FILE UPDATES: 27 JUN 2005 HIGHEST RN 853049-67-9
 DICTIONARY FILE UPDATES: 27 JUN 2005 HIGHEST RN 853049-67-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

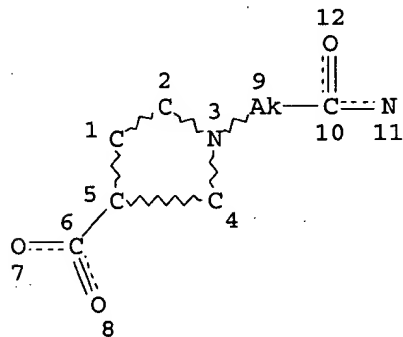
 *
 * The CA roles and document type information have been removed from *
 * the IDE default display format and the ED field has been added, *
 * effective March 20, 2005. A new display format, IDERL, is now *
 * available and contains the CA role and document type information. *
 *

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
 information enter HELP PROP at an arrow prompt in the file or refer
 to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que l61

L5 STR

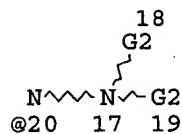
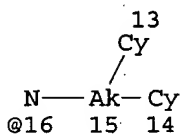


NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RSPEC 3
 NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

The chemical structure is 1-azabicyclo[3.2.0]hept-5-en-2-one. It consists of a five-membered ring with a nitrogen atom (N) at position 3, a carbonyl group (C=O) at position 2, and a double bond between carbons 5 and 6. A side chain is attached to the nitrogen atom at position 3, consisting of a carbon atom (C) double-bonded to an oxygen atom (O) and single-bonded to a group labeled G1. The atoms are numbered 1 through 12. The labels HO, O, and Ak are also present.



Cy @21

22 ANSWERS

L8	6 S	(US94-293349# OR US94-334717# OR US95-442575# OR US95-497998#
L9	1 S	US2000-653563#/AP,PRN
	E	WINN M/AU
L10	155 S	E3-E9,E13
	E	BOYD S/AU

L11 101 S E3,E4
 E BOYD STEVE/AU
 L12 60 S E4,E5
 E HUTCHINS C/AU
 L13 70 S E3,E10,E13,E16,E17
 E JAE H/AU
 L14 43 S E5,E13,E14
 E TASKER A/AU
 L15 63 S E3,E8,E9
 E ON GELDERN T/AU
 E VON GELDERN T/AU
 L16 92 S E3-E8
 E VONGELDERN T/AU
 L17 3 S E4
 E GELDERN T/AU
 L18 1 S E4
 E KESTER J/AU
 L19 25 S E3,E11-E14
 E SORENSEN B/AU
 L20 16 S E3,E8
 L21 40 S E46
 E SZCZEPANKIEWICZ B/AU
 L22 43 S E4-E7
 E HENRY K/AU
 E SZCZEPANKIEWICZ B/AU
 L23 1 S E2
 E HENRY K/AU
 L24 15 S E3,E7
 L25 34 S E35,E37-E39
 E LIU G/AU
 L26 843 S E3-E29
 E LIU GANG/AU
 L27 869 S LIU GANG?/AU
 E WITTENBERGER S/AU
 L28 61 S E4-E8
 E KING S/AU
 L29 54 S E3,E4
 E KING STEVE/AU
 L30 71 S E3,E4,E7-E9
 E JANUS T/AU
 L31 15 S E4,E6,E7
 E PADLEY R/AU
 L32 28 S E4-E6
 E ABBOT/PA,CS
 L33 147 S E3,E4
 E ABBOTT/PA,CS
 L34 8778 S E3,E4
 L35 197 S L7
 L36 1 S L9 AND L35
 L37 54 S L8-L34 AND L35
 L38 54 S L36,L37
 L39 0 S L38 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
 L40 6 S L35 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
 L41 10 S L35 AND (PY<=1995 AND PRY<=1995 OR AY<=1995)
 L42 3 S L38 AND L41
 L43 7 S L41 NOT L42
 L44 2 S L43 NOT 74/SC,SX
 L45 4 S L36,L42

FILE 'REGISTRY' ENTERED AT 15:34:48 ON 28 JUN 2005

jan delaval - 28 june 2005

FILE 'HCAPLUS' ENTERED AT 15:35:13 ON 28 JUN 2005
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SET SMARTSELECT OFF

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L48 2273 S L7 AND L47

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L49 SEL L36 1- RN : 669 TERMS
SET SMARTSELECT OFF

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L50 669 S L49
L51 287 S L7 AND L50
L52 0 S L1 CSS SAM SUB=L7
L53 7 S L1 CSS FUL SUB=L7
SAV L53 SHIAO653A/A

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L54 0 S L53

FILE 'HCAPLUS' ENTERED AT 15:38:30 ON 28 JUN 2005
L55 3 S L53
S L55 AND L1-L34

FILE 'REGISTRY' ENTERED AT 15:38:43 ON 28 JUN 2005

FILE 'HCAPLUS' ENTERED AT 15:38:44 ON 28 JUN 2005
L56 2 S L55 AND L8-L34
E HWAN SOO/AU
L57 1 S E5
E HWAN S/AU
L58 2 S L56,L57

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L59 0 S L53

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L60 STR L1
L61 22 S L60 CSS FUL SUB=L7
SAV L61 SHIAO653B/A

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L62 0 S L61

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L64 2 S L63 AND L8-L34,L56-L58
L65 1 S L63 NOT L64

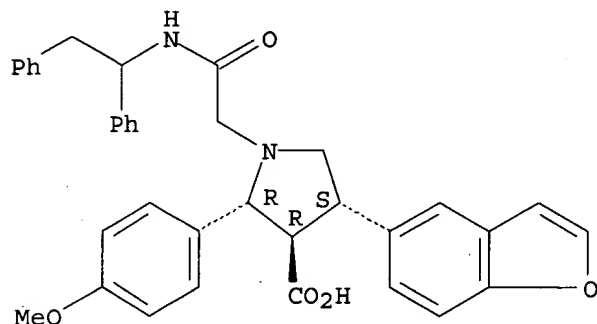
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L66 0 S L61

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=> d ide can tot l61

L61 ANSWER 1 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 697767-60-5 REGISTRY
 ED Entered STN: 23 Jun 2004
 CN 3-Pyrrolidinecarboxylic acid, 4-(5-benzofuranyl)-1-[2-[(1,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C36 H34 N2 O5
 SR CA
 LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

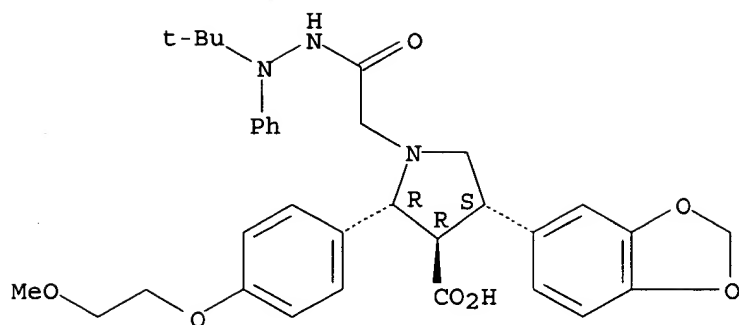
REFERENCE 1: 141:16897

L61 ANSWER 2 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 403614-32-4 REGISTRY
 ED Entered STN: 31 Mar 2002
 CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α -[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel-, monoacetate (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C33 H39 N3 O7 . C2 H4 O2
 SR CA
 LC STN Files: CA, CAPLUS

CM 1

CRN 403614-31-3
 CMF C33 H39 N3 O7

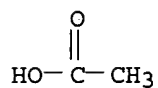
Relative stereochemistry.



CM 2

CRN 64-19-7

CMF C2 H4 O2



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

L61 ANSWER 3 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN

RN 403614-31-3 REGISTRY

ED Entered STN: 31 Mar 2002

CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α -[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

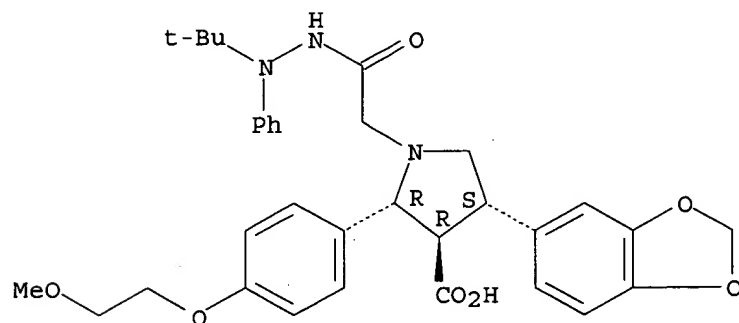
MF C33 H39 N3 O7

CI COM

SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.



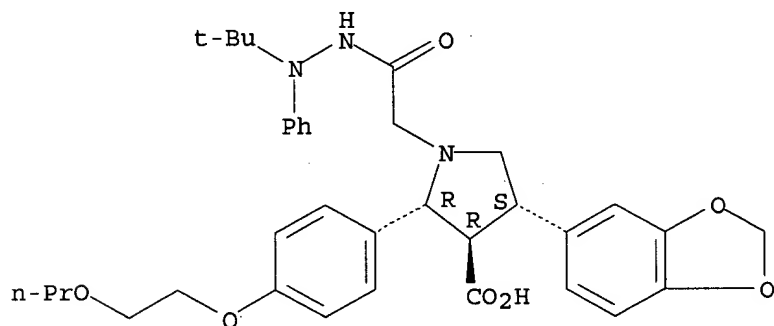
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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

L61 ANSWER 4 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-30-2 REGISTRY
ED Entered STN: 31 Mar 2002
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-propoxyethoxy)phenyl]-, α -[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H43 N3 O7
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



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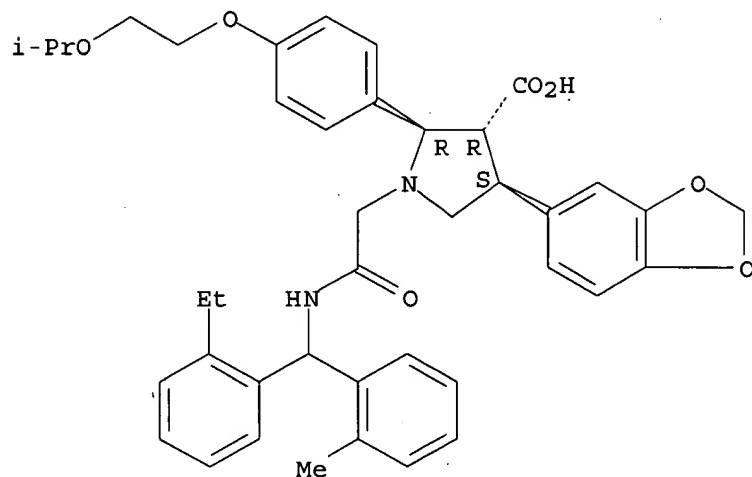
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L61 ANSWER 5 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-29-9 REGISTRY
ED Entered STN: 31 Mar 2002
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H46 N2 O7 . C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 246853-83-8
CMF C41 H46 N2 O7

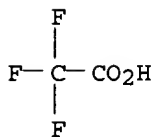
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

L61 ANSWER 6 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN

RN 403614-26-6 REGISTRY

ED Entered STN: 31 Mar 2002

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel-, trifluoroacetate (5:1) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C38 H40 N2 O7 . 1/5 C2 H F3 O2

SR CA

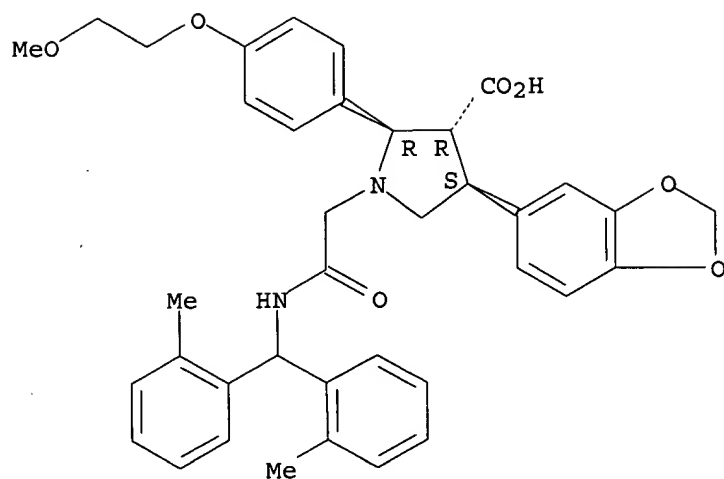
LC STN Files: CA, CAPLUS

CM 1

CRN 246853-81-6

CMF C38 H40 N2 O7

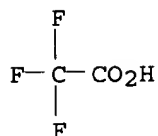
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



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REFERENCE 1: 136:232311

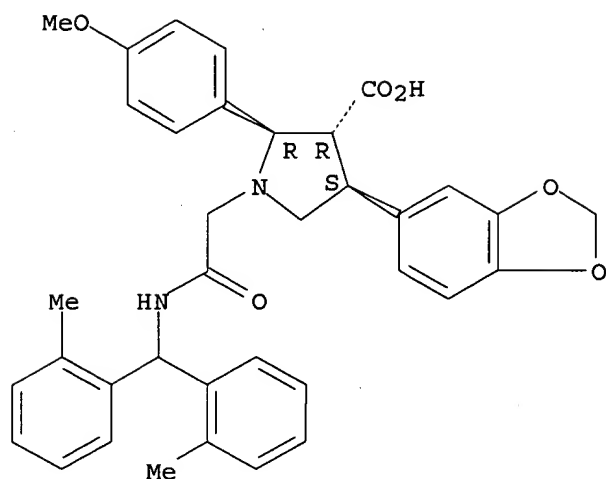
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 ED Entered STN: 31 Mar 2002
 CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, trifluoroacetate (5:2) (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C36 H36 N2 O6 . 2/5 C2 H F3 O2
 SR CA
 LC STN Files: CA, CAPLUS

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CRN 246853-46-3

CMF C36 H36 N2 O6

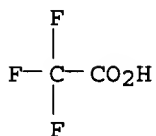
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

L61 ANSWER 8 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN

RN 246853-85-0 REGISTRY

ED Entered STN: 09 Nov 1999

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)

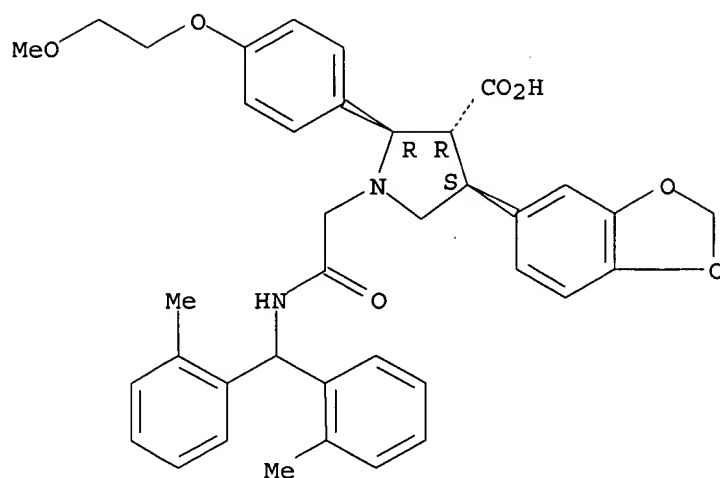
FS STEREOSEARCH

MF C38 H40 N2 O7

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



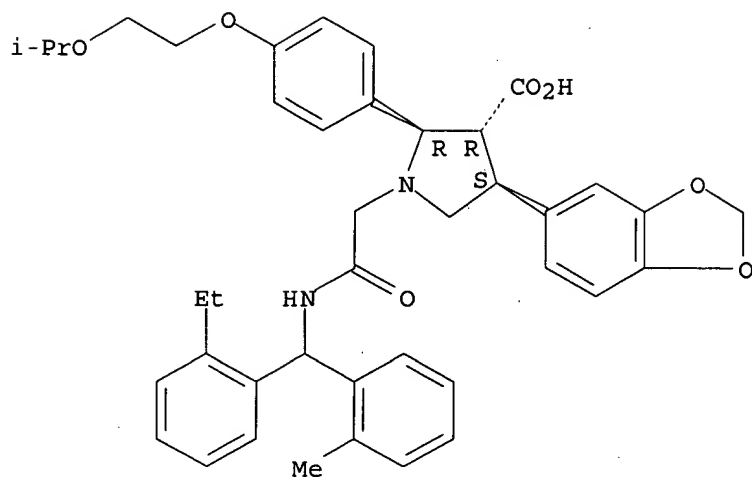
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 9 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-83-8 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[[2-[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H46 N2 O7
CI COM
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

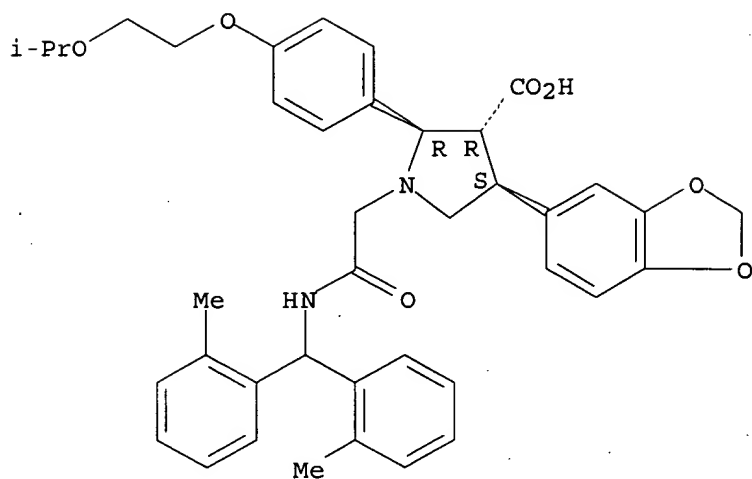
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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

REFERENCE 2: 131:286357

L61 ANSWER 10 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-82-7 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H44 N2 O7
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



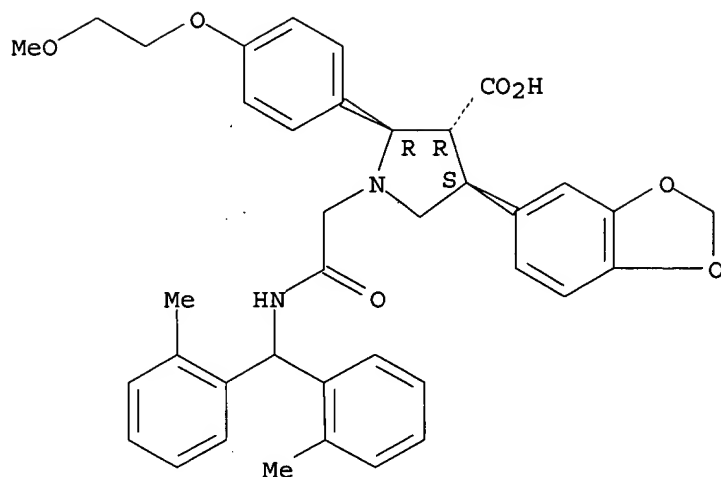
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 11 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-81-6 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H40 N2 O7
CI COM
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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REFERENCE 1: 136:232311

REFERENCE 2: 131:286357

L61 ANSWER 12 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN

RN 246853-66-7 REGISTRY

ED Entered STN: 09 Nov 1999

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-ethylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C38 H40 N2 O6 . C2 H F3 O2

SR CA

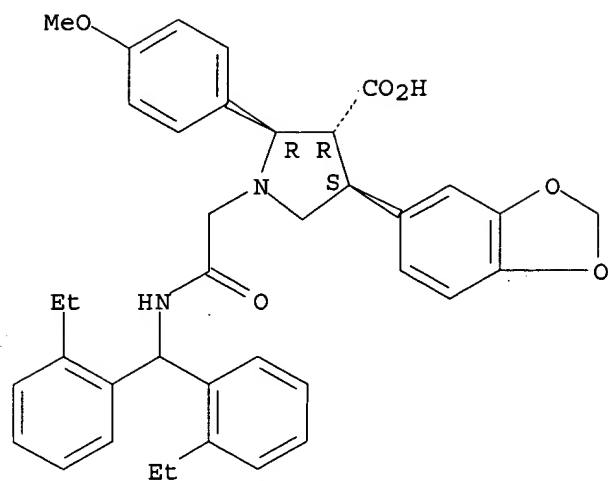
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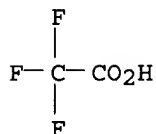
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 13 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN

RN 246853-65-6 REGISTRY

ED Entered STN: 09 Nov 1999

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-ethylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

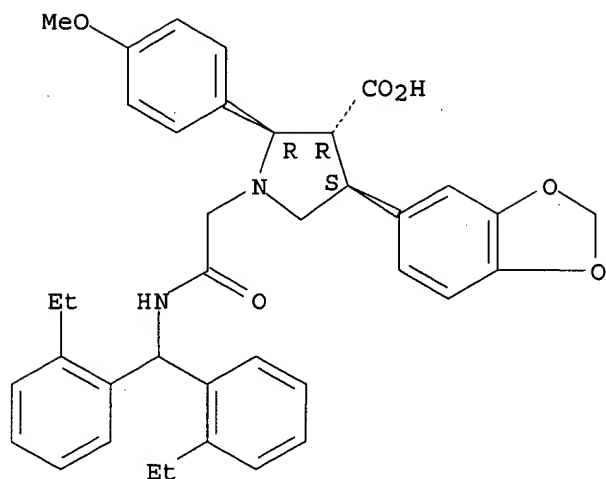
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MF C38 H40 N2 O6

CI COM

SR CA

Relative stereochemistry.



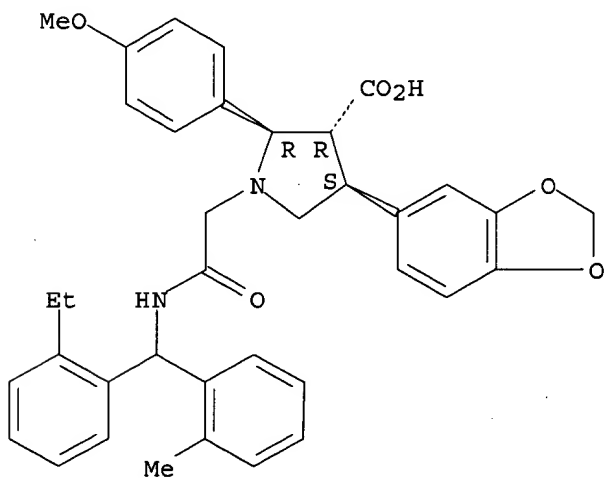
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L61 ANSWER 14 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
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 CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C37 H38 N2 O6 . C2 H F3 O2
 SR CA
 LC STN Files: CA, CAPLUS

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CRN 246853-63-4
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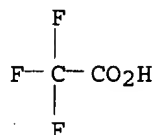
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 15 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN

RN 246853-63-4 REGISTRY

ED Entered STN: 09 Nov 1999

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[2-ethylphenyl](2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

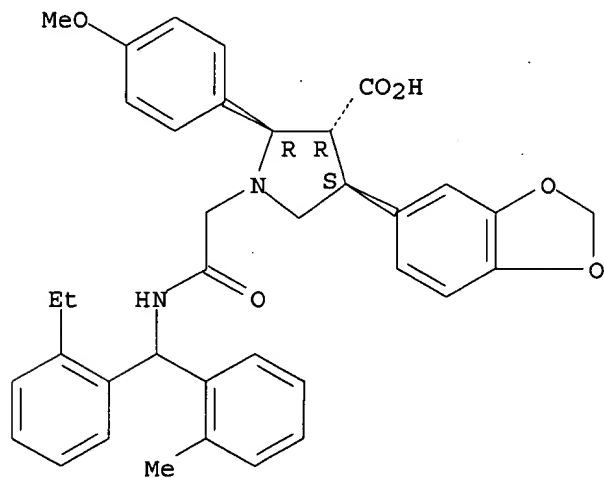
FS STEREOSEARCH

MF C37 H38 N2 O6

CI COM

SR CA

Relative stereochemistry.



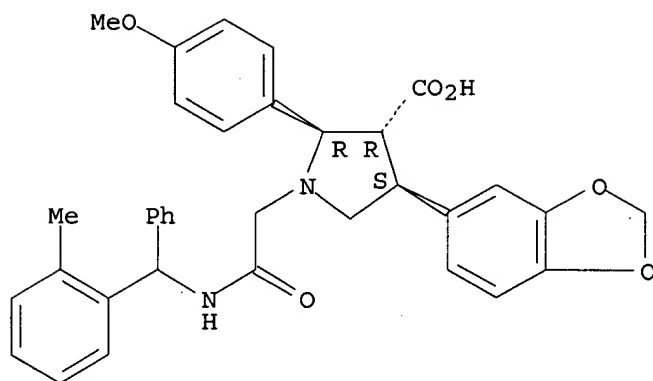
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L61 ANSWER 16 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN

RN 246853-61-2 REGISTRY

ED Entered STN: 09 Nov 1999

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[2,5-



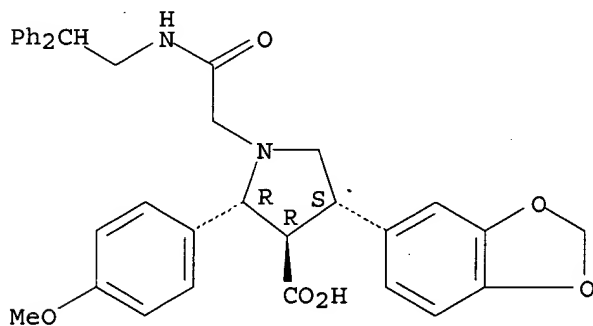
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 18 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-58-7 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(2,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H34 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



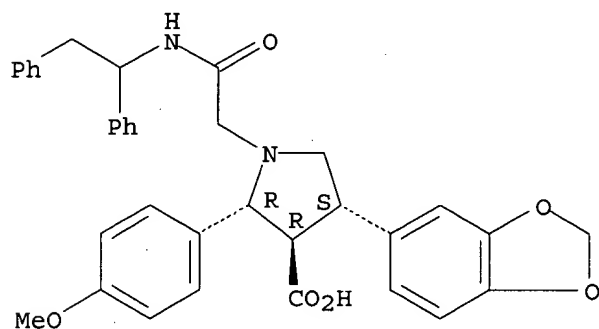
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 19 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-57-6 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(1,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H34 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



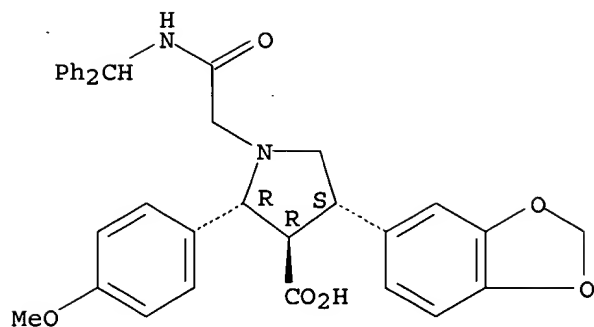
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 20 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-55-4 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(diphenylmethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H32 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



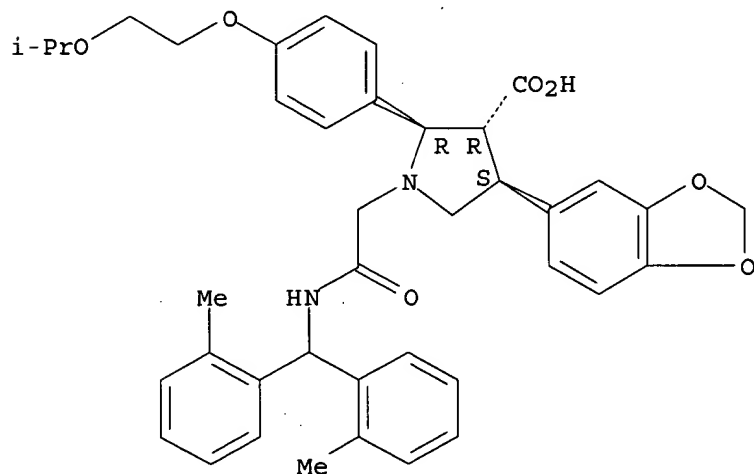
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 21 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-53-2 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H44 N2 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



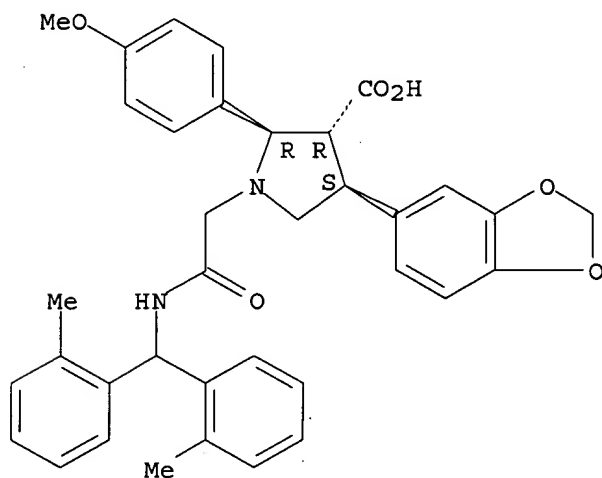
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 22 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-46-3 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-,
(2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H36 N2 O6
CI COM
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

REFERENCE 2: 131:286357

=> fil hcaplus

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FILE LAST UPDATED: 27 Jun 2005 (20050627/ED)

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L65 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:322089 HCAPLUS

DN 141:16897

ED Entered STN: 21 Apr 2004

TI Chemical Function Based Pharmacophore Generation of Endothelin-A Selective Receptor Antagonists

AU Funk, Oliver F.; Kettmann, Viktor; Drimal, Jan; Langer, Thierry

CS Department of Pharmaceutical, Chemistry Institute of Pharmacy, University of Innsbruck, Innsbruck, A-6020, Austria

SO Journal of Medicinal Chemistry (2004), 47(11), 2750-2760

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

CC 1-3 (Pharmacology)

AB Both quant. and qual. chemical function based pharmacophore models of endothelin-A (ETA) selective receptor antagonists were generated by using the two algorithms HypoGen and HipHop, resp., which are implemented in the Catalyst mol. modeling software. The input for HypoGen is a training set of 18 ETA antagonists exhibiting IC50 values ranging between 0.19 nM and 67 µM. The best output hypothesis consists of five features: two hydrophobic (HY), one ring aromatic (RA), one hydrogen bond acceptor (HBA), and one neg. ionizable (NI) function. The highest scoring Hip Hop model consists of six features: three hydrophobic (HY), one ring aromatic (RA), one hydrogen bond acceptor (HBA), and one neg. ionizable (NI). It is the result of an input of three highly active, selective, and structurally diverse ETA antagonists. The predictive power of the quant. model could be approved by using a test set of 30 compds., whose activity values spread over 6 orders of magnitude. The two pharmacophores were tested according to their ability to extract known endothelin antagonists from the 3D mol. structure database of Derwent's World Drug Index. Thereby the main part of selective ETA antagonistic entries was detected by the two hypotheses. Furthermore, the pharmacophores were used to screen the Maybridge database. Six compds. were chosen from the output hit lists for in vitro testing of their ability to displace endothelin-1 from its receptor. Two of these are new potential lead compds. because they are structurally novel and exhibit satisfactory activity in the binding assay.

ST pharmacophore endothelin A receptor binding structure screening drug design; Maybridge database screening algorithm pharmacophore endothelin A receptor antagonist; mol modeling endothelin A receptor antagonist QSAR prediction

IT Computer program

(Catalyst mol. modeling; chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT Algorithm
(HipHop; chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT Algorithm
(HypoGen; chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT Databases
(Maybridge; chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT Drug design
Drug screening
Molecular modeling
Pharmacophores
QSAR (structure-activity relationship)
(chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT Structure-activity relationship
(receptor-binding, endothelin-A; chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT Endothelin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type ETA; chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT 123626-67-5, Endothelin-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

IT 155561-67-4 158692-14-9 173864-15-8 173864-16-9 173937-91-2
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697767-54-7 697767-55-8 697767-56-9 697767-57-0 697767-58-1
697767-59-2 697767-60-5 697767-61-6 697767-62-7
697767-63-8 697767-64-9 697767-65-0 697767-66-1 697767-67-2
697767-68-3 697767-69-4 697767-70-7 697767-71-8 697800-66-1, S
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD

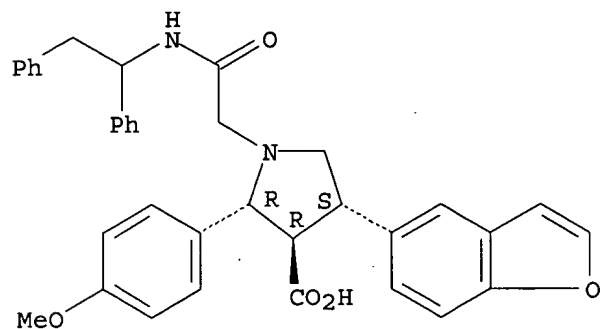
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- IT 697767-60-5
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (chemical function based pharmacophore generation of endothelin-A selective receptor antagonists)

RN 697767-60-5 HCAPLUS
 CN 3-Pyrrolidinecarboxylic acid, 4-(5-benzofuranyl)-1-[2-[(1,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

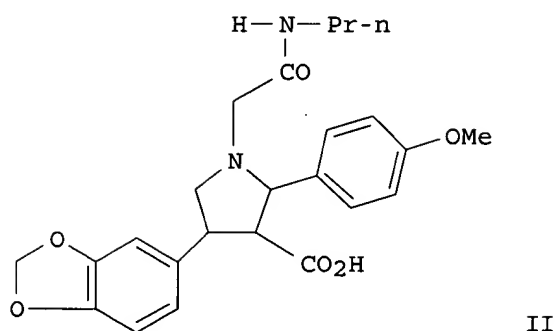
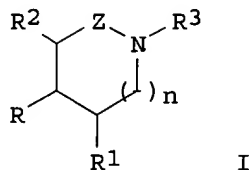


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L64 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:171682 HCAPLUS
 DN 136:232311
 ED Entered STN: 08 Mar 2002
 TI Preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivatives as endothelin antagonists
 IN Winn, Martin; Boyd, Steven A.; Hutchins, Charles W.; Hwan-Soo, Jae; Tasker, Andrew S.; Von Geldern, Tomas W.; Kester, Jeffrey; Sorensen, Bryan K.; Szczepankiewicz, Bruce G.; Henry, Kenneth; Liu, Gang; Wittenberger, Steven J.; King, Steven A.; Janus, Todd J.; Padley, Robert J.
 PA Abbott Laboratories, USA
 SO PCT Int. Appl., 817 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-4025
 ICS A61P009-12; C07D405-04
 CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63
 FAN.CNT 1

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WO 2002017912	A1	20020307	WO 2001-US27220	20010831 <--
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
PRAI US 2000-653563	A	20000831	<--	
CLASS				
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES		
WO 2002017912	ICM	A61K031-4025		
	ICS	A61P009-12; C07D405-04		
WO 2002017912	ECLA	C07D405/04+317+207		

OS MARPAT 136:232311
GI



AB Title compds. [I; n = 0; Z = CH₂; R = CO₂H; R₁ = alkoxyaryl, alkoxyalkoxyaryl, heterocyclalkyl; R₂ = 1,3-benzodioxyl, 4-benzofuranyl, 5-indanyl; R₃ = R₄R₅CO; R₄ = R₆R₇N, R₈R₉NNH; R₅ = methylene; one of R₆, R₇ is H, the other is arylalkyl, diarylalkyl; one of R₈, R₉ is alkyl, the other is aryl] stereoisomers, and pharmaceutically acceptable salts are prepared as endothelin antagonists. Thus, the title compound II was prepared from Et (4-methoxybenzoyl)acetate, 5-(2-nitrovinyl)-1,3-benzodioxol, ethyldiisopropylamine, and N-Pr bromoacetamide and was in vitro tested for binding effect to the endothelin receptor and the determination of title compound as functional ET antagonist.

ST benzodioxolyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist; oxopyrimidinylethyl benzodioxolyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist; indanyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist; benzofuranyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist

IT Endothelin receptors

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(preparation of 4-benzoheterocycl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT 116243-73-3, Endothelin

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(preparation of 4-benzoheterocycl-1-aminocarbonylmethylpyrrolidine-3-

carboxylic acid derivs. as endothelin antagonists)

IT 195708-83-9P
 RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)
 (preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT 173864-16-9P 178608-45-2P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

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 178609-00-2P 178609-01-3P 178609-03-5P 178609-04-6P 178609-05-7P
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 195705-03-4P 195705-05-6P 195705-08-9P 195705-16-9P 195705-19-2P
 195705-22-7P 195705-30-7P 195705-34-1P 195705-37-4P 195705-39-6P
 195705-41-0P 195705-45-4P 195705-50-1P 195705-53-4P 195705-55-6P
 195705-61-4P 195705-64-7P 195705-67-0P 195705-70-5P 195705-78-3P
 195705-81-8P 195705-83-0P 195705-85-2P 195705-87-4P 195705-89-6P
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 195706-15-1P 195706-16-2P 195706-17-3P 195706-21-9P 195706-22-0P
 195706-24-2P 195706-25-3P 195706-26-4P 195706-28-6P 195706-29-7P
 195706-30-0P 195706-31-1P 195706-33-3P 195706-34-4P 195706-35-5P
 195706-37-7P 195706-38-8P 195706-39-9P 195706-40-2P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT	195706-41-3P	195706-42-4P	195706-43-5P	195706-45-7P	195706-46-8P
	195706-47-9P	195706-48-0P	195706-50-4P	195706-52-6P	195706-53-7P
	195706-54-8P	195706-55-9P	195706-56-0P	195706-57-1P	195706-60-6P
	195706-61-7P	195706-62-8P	195706-63-9P	195706-67-3P	195706-69-5P
	195706-71-9P	195706-73-1P	195706-75-3P	195706-77-5P	195706-79-7P
	195706-81-1P	195706-82-2P	195706-84-4P	195706-86-6P	195706-90-2P
	195706-91-3P	195706-92-4P	195706-94-6P	195706-95-7P	195706-96-8P
	195706-97-9P	195706-99-1P	195707-01-8P	195707-02-9P	195707-05-2P
	195707-07-4P	195707-08-5P	195707-09-6P	195707-12-1P	195707-13-2P
	195707-14-3P	195707-16-5P	195707-17-6P	195707-22-3P	195707-27-8P
	195707-28-9P	195707-29-0P	195707-31-4P	195707-32-5P	195707-33-6P
	195707-34-7P	195707-35-8P	195707-36-9P	195707-45-0P	195707-55-2P
	195707-57-4P	195707-67-6P	195707-77-8P	195733-43-8P	209188-79-4P
	209188-84-1P	209188-86-3P	209188-93-2P	209188-98-7P	209189-03-7P
	209189-06-0P	209189-08-2P	209189-18-4P	209189-28-6P	209189-35-5P
	209191-55-9P	212480-90-5P	212481-07-7P	212481-47-5P	212481-50-0P
	212481-67-9P	220482-25-7P	220482-87-1P	220483-95-4P	220484-35-5P
	220484-97-9P	220488-20-0P	220489-14-5P	220491-11-2P	220492-06-8P
	220496-18-4P	220503-20-8P	220503-25-3P	220503-27-5P	220503-30-0P
	220503-57-1P	220503-60-6P	220584-47-4P	220584-48-5P	220584-52-1P
	239098-16-9P	239098-29-4P	239098-30-7P	246853-46-3P	
	246853-76-9P	246853-77-0P	246853-80-5P	246853-81-6P	
	246853-83-8P	313245-83-9P	313245-91-9P	313246-12-7P	
	313246-27-4P	313246-33-2P	313246-36-5P	313246-38-7P	313246-43-4P
	313246-46-7P	313246-49-0P	313246-52-5P	313246-55-8P	313246-60-5P
	313246-63-8P	313246-66-1P	313246-69-4P	313246-72-9P	313246-74-1P
	313246-83-2P	313246-86-5P	313246-95-6P	313247-01-7P	313247-04-0P
	313247-20-0P	313247-27-7P	313247-34-6P	403613-82-1P	403613-86-5P
	403613-87-6P	403613-89-8P	403613-90-1P	403613-91-2P	403613-92-3P
	403613-93-4P	403613-94-5P	403613-95-6P	403613-96-7P	403613-97-8P
	403613-98-9P	403613-99-0P	403614-00-6P	403614-01-7P	403614-02-8P
	403614-03-9P	403614-05-1P	403614-07-3P	403614-08-4P	403614-10-8P
	403614-12-0P	403614-13-1P	403614-14-2P	403614-15-3P	403614-16-4P
	403614-17-5P	403614-18-6P	403614-19-7P	403614-20-0P	403614-21-1P
	403614-22-2P	403614-23-3P	403614-24-4P	403614-25-5P	
	403614-26-6P	403614-27-7P	403614-28-8P	403614-29-9P	
	403614-30-2P	403614-31-3P	403614-32-4P		
	403657-02-3P				

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT	66-77-3, Naphthalene-1-carboxaldehyde	66-99-9, Naphthalene-2-carboxaldehyde	75-64-9, reactions	78-39-7, Triethyl orthoacetate
	79-03-8, Propionyl chloride	79-30-1, Isobutyryl chloride	94-02-0, Ethyl benzoylacetate	96-48-0, γ-Butyrolactone
	98-10-2, Benzenesulfonamide	99-66-1, 2-Propylpentanoic acid	100-06-1, 100-52-7, Benzaldehyde	reactions
	100-69-6, 2-Vinylpyridine	103-71-9, Phenyl isocyanate	reactions	106-41-2, 4-Bromophenol
	107-03-9, 1-Propanethiol	107-10-8, Propylamine	reactions	107-86-8, 3-Methyl-2-butenal
	107-87-9, 2-Pentanone	108-10-1, 4-Methyl-2-pentanone	109-73-9, n-Butylamine	reactions
	109-90-0, Ethyl isocyanate	111-36-4, Butyl isocyanate	111-92-2, Dibutylamine	120-14-9, 3,4-Dimethoxybenzaldehyde
	120-57-0, Piperonal	123-08-0, 4-Hydroxybenzaldehyde	123-11-5, 4-Methoxybenzaldehyde	reactions
	123-19-3, 4-Heptanone	141-75-3, Butyryl chloride	141-97-9, Ethyl	

acetoacetate 142-84-7, Dipropylamine 144-48-9, Iodoacetamide
 328-38-1, D-Leucine 455-88-9, 2-Fluoro-5-nitrotoluene 455-91-4
 459-46-1, 4-Fluorobenzyl bromide 459-57-4, 4-Fluorobenzaldehyde
 496-16-2, 2,3-Dihydrobenzofuran 527-69-5, 2-Furoyl chloride 541-41-3,
 Ethyl chloroformate 542-69-8, 1-Iodobutane 574-98-1 590-86-3,
 Isovaleraldehyde 591-20-8, 3-Bromophenol 591-31-1,
 3-Methoxybenzaldehyde 592-55-2, 2-Bromoethyl ethyl ether 598-72-1,
 2-Bromopropanoic acid 613-45-6, 2,4-Dimethoxybenzaldehyde 615-20-3,
 2-Chlorobenzothiazole 693-07-2, 2-Chloroethyl ethyl sulfide 1018-97-9,
 2,2'-Dimethylbenzophenone 1126-78-9, N-Butyl aniline 1191-99-7,
 2,3-Dihydrofuran 1196-70-9, Indole-6-carboxaldehyde 1877-77-6,
 3-Aminobenzyl alcohol 2032-35-1, Bromoacetaldehyde diethyl acetal
 2386-60-9, 1-Butanesulfonyl chloride 2859-68-9, 3-(2-Pyridyl)-propanol
 3085-68-5, N,N-Diallyl acrylamide 3179-10-0, 4-(2-Nitrovinyl)anisole
 3182-95-4, (S)-Phenylalaninol 3249-68-1, Ethyl butyrylacetate
 3840-30-0, 3,4,5-Trimethoxybenzyl chloride 3934-20-1,
 2,4-Dichloropyrimidine 4595-60-2, 2-Bromopyrimidine 5292-43-3,
 tert-Butyl bromoacetate 5395-67-5, N-Propyl bromoacetamide 5416-93-3,
 4-Methoxyphenyl isocyanate 5695-63-6, 2-Bromomethyl-1,3-dioxane
 5780-07-4, 5-Methoxypiperonal 6291-85-6, 3-Ethoxypropylamine 7087-68-5
 7152-15-0, Ethyl isobutyrylacetate 7663-76-5 10035-16-2,
 Benzofuran-5-carboxaldehyde 10147-36-1, Propylsulfonyl chloride
 10147-37-2, 2-Propanesulfonyl chloride 10554-65-1, 6-(2-Nitrovinyl)-1,4-
 benzodioxane 13358-73-1, Dibutylcarbonyl chloride 15159-40-7,
 4-Morpholinocarbonyl chloride 18495-25-5, 1-Bromo-2-hexyne 20261-68-1,
 1-Chloro-2-hexanone 23590-03-6, N,N-Dibutyl glycine 24074-26-8,
 Diisopropyl(ethoxycarbonylmethyl)phosphonate 34036-07-2,
 3,4-Difluorobenzaldehyde 38945-21-0, O-Allylhydroxylamine hydrochloride
 42149-74-6, 2-Chloroethyl propyl ether 51445-11-5 51932-70-8,
 Indan-4-carboxaldehyde 54149-17-6, 2-(2-Methoxyethoxy)ethyl bromide
 55745-70-5, 2,3-Dihydrobenzofuran-5-carboxaldehyde 63131-29-3, Methyl
 (4-fluorobenzoyl)acetate 73873-61-7, trans-4-Methoxycyclohexane
 carboxylic acid 81581-27-3, Ethyl (1,3-benzodioxol-5-ylcarbonyl)acetate
 90719-32-7, (S)-4-Benzyl-2-oxazolidinone 101498-88-8, Ethyl
 (4-tert-butylbenzoyl)acetate 110874-83-4, Methyl 3-oxo-6-octenoate
 116169-12-1, Ethyl 3,3-dimethylhexanoate 134414-16-7, N-Butyl-N-methyl
 bromoacetamide 158692-25-2 178609-50-2 178609-64-8,
 N-Methyl-N-propyl bromoacetamide 178609-65-9, Ethyl (4-methoxy-2-
 (methoxymethoxybenzoyl)acetate 178609-66-0, N-(3,4-Dimethoxybenzyl)
 2-bromoacetamide 178609-67-1 178609-68-2 220584-69-0 220584-95-2
 288309-52-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 4-benzoheterocycl-1-aminocarbonylmethylpyrrolidine-3-
 carboxylic acid derivs. as endothelin antagonists)

IT 111-75-1P, N-Butyl-N-(2-hydroxyethyl)amine 452-69-7P,
 4-Fluoro-3-methylaniline 589-55-9P, 4-Heptanol 937-33-7P 1485-00-3P
 1589-35-1P, trans-5-Methylhex-2-en-1-ol 2881-83-6P 4325-82-0P,
 4-Methyl-3-penten-2-ol 4543-95-7P 5326-87-4P, N-Phenylbromoacetamide
 6303-18-0P, 1-Pentanesulfonyl chloride 15197-75-8P, 2-Pyridinepropanoic
 acid 15896-78-3P 17664-93-6P, D-Leucine benzyl ester tosylate
 22568-48-5P 24066-72-6P 24642-84-0P 25560-11-6P 30084-91-4P,
 Indan-5-carboxaldehyde 34993-63-0P 36171-18-3P 40124-27-4P,
 N,N-Dibutylbromoacetamide 41692-47-1P, Ethyl 3-methylhexanoate
 42042-67-1P, N-Butyl-4-hydroxybutyramide 67764-22-1P 77191-38-9P
 81042-10-6P 89532-73-0P, 3-(1-Pyrazolyl)-propionic acid 90843-31-5P,
 5-Acetyl-2,3-dihydrobenzofuran 95333-13-4P, Benzofuran-4-carboxaldehyde
 100366-94-7P 103335-72-4P 123297-88-1P, Benzofuran-6-carboxaldehyde
 149673-73-4P 173864-36-3P 173864-45-4P 173864-46-5P 173864-47-6P
 173864-48-7P 173937-93-4P 178609-16-0P 178609-18-2P 178609-21-7P
 178609-22-8P 178609-24-0P 178609-26-2P, 1-Chloro-3-propyl-2-hexanone

178609-27-3P	178609-28-4P	178609-33-1P	178609-38-6P	178609-42-2P
178609-44-4P	178609-45-5P	178609-47-7P	178609-48-8P	178609-54-6P
178609-55-7P	178609-57-9P	178609-60-4P	178609-61-5P	178609-63-7P
178739-03-2P	178739-07-6P	195510-46-4P	195510-85-1P	195707-78-9P
195707-83-6P	195707-84-7P	195708-01-1P	195708-08-8P	195708-10-2P
195708-11-3P	195708-12-4P	195708-13-5P	195708-14-6P	195708-15-7P
195708-16-8P	195708-17-9P	195708-18-0P	195708-19-1P	195708-21-5P
195708-24-8P	195708-25-9P	195708-26-0P	195708-27-1P	195708-28-2P
195708-29-3P	195708-31-7P	195708-33-9P	195708-35-1P	195708-36-2P
195708-37-3P	195708-39-5P	195708-63-5P	195708-78-2P	195708-80-6P
204452-94-8P	209214-13-1P	209214-15-3P	209214-29-9P	209214-30-2P
209214-33-5P	209408-46-8P	209408-54-8P	212480-23-4P	212481-92-0P
212482-48-9P	220524-44-7P	220534-18-9P	220543-19-1P	220584-80-5P
220584-81-6P	220584-87-2P	220584-88-3P	220584-89-4P	220584-99-6P
220585-00-2P	246853-44-1P	246853-45-2P	246853-47-4P	313247-57-3P
313247-85-7P	313247-88-0P	403614-33-5P	403614-35-7P	403614-36-8P
403614-37-9P	403614-38-0P	403614-39-1P	403614-40-4P	403614-41-5P
403614-42-6P	403614-43-7P	403614-44-8P	403614-45-9P	403614-46-0P
403614-47-1P	403614-49-3P	403614-50-6P	403657-03-4P	403657-04-5P
403657-05-6P				

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Abbott Lab; WO 9606095 A 1996 HCAPLUS
- (2) Abbott Lab; WO 9730045 A 1997 HCAPLUS
- (3) Abbott Lab; WO 9730046 A 1997 HCAPLUS
- (4) Liu, G; J MED CHEM 1999, V42(18), P3679 HCAPLUS

IT 246853-46-3P 246853-81-6P 246853-83-8P
403614-24-4P 403614-26-6P 403614-29-9P
403614-30-2P 403614-31-3P 403614-32-4P

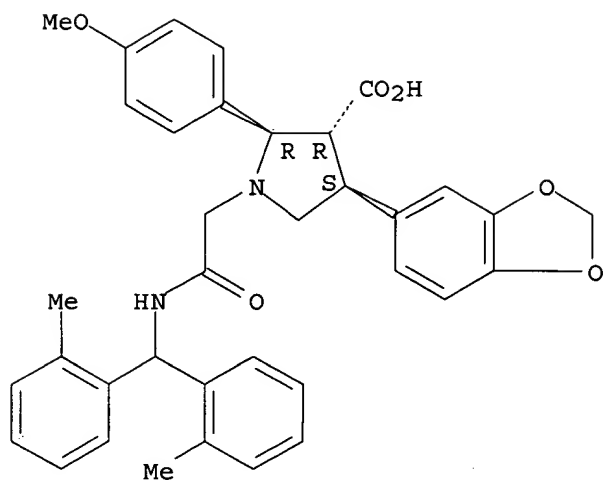
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

RN 246853-46-3 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

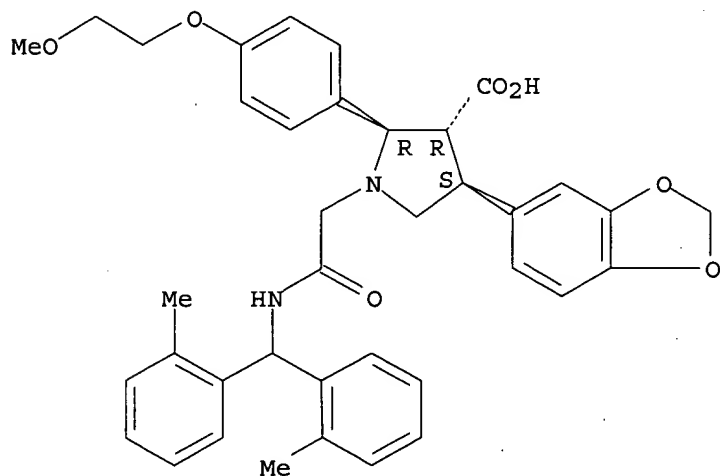
Relative stereochemistry.



RN 246853-81-6 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

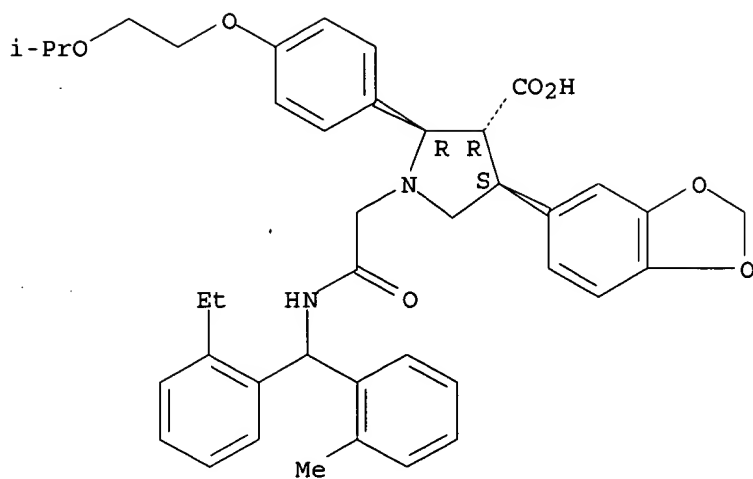
Relative stereochemistry.



RN 246853-83-8 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 403614-24-4 HCAPLUS

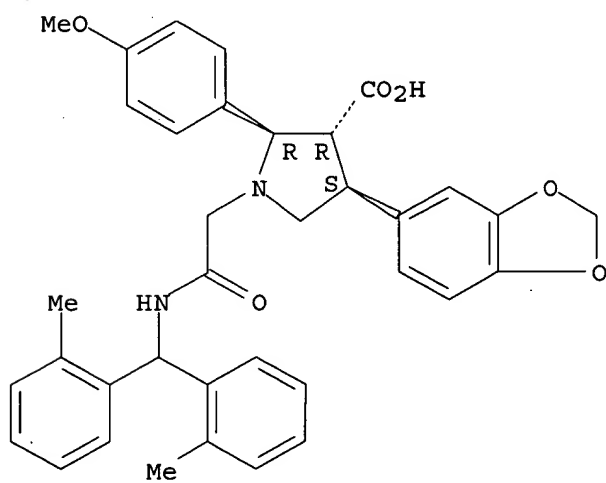
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, trifluoroacetate (5:2) (9CI) (CA INDEX NAME)

CM 1

CRN 246853-46-3

CMF C36 H36 N2 O6

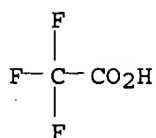
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 403614-26-6 HCAPLUS

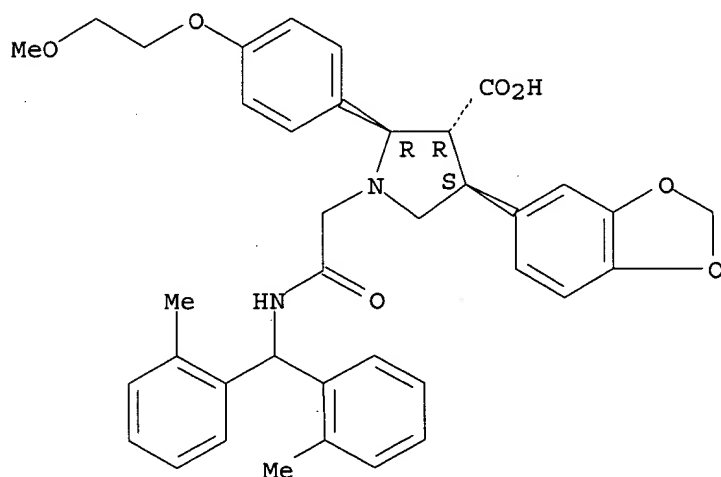
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel-, trifluoroacetate (5:1) (9CI) (CA INDEX NAME)

CM 1

CRN 246853-81-6

CMF C38 H40 N2 O7

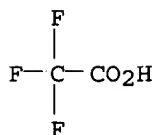
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



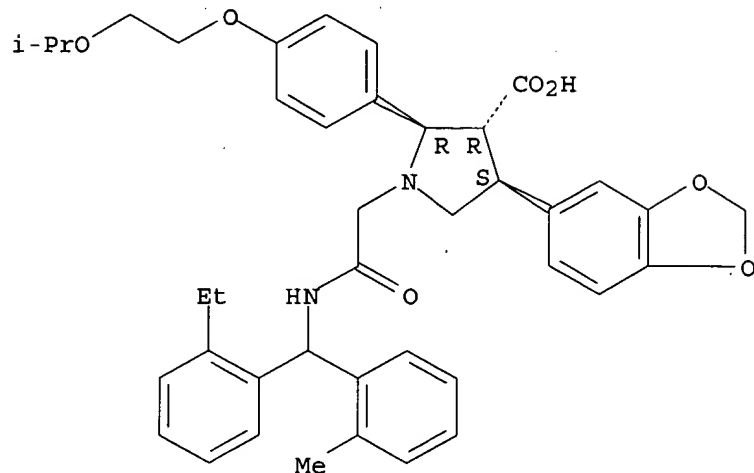
RN 403614-29-9 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

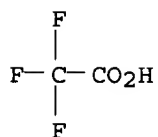
CRN 246853-83-8
CMF C41 H46 N2 O7

Relative stereochemistry.



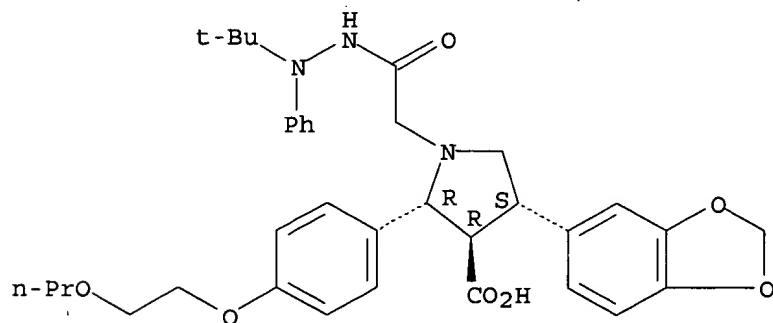
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 403614-30-2 HCAPLUS
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-propoxyethoxy)phenyl]-, α-[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

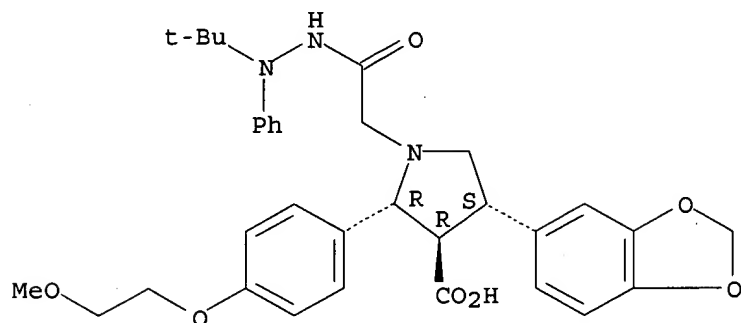
Relative stereochemistry.



RN 403614-31-3 HCAPLUS

CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α -[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 403614-32-4 HCAPLUS

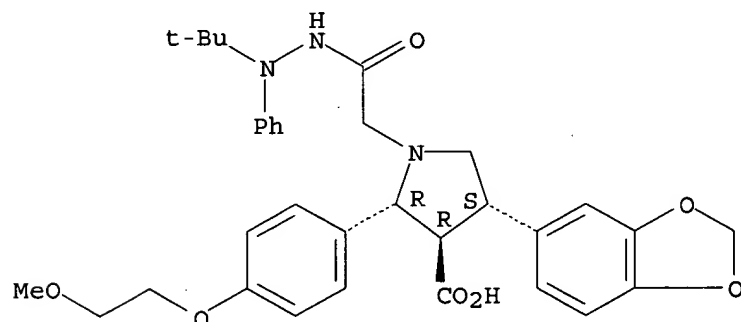
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α -[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 403614-31-3

CMF C33 H39 N3 O7

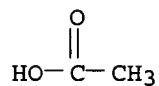
Relative stereochemistry.



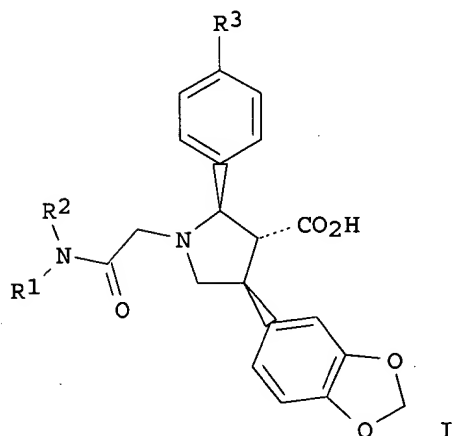
CM 2

CRN 64-19-7

CMF C2 H4 O2



L64 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1999:510837 .HCAPLUS
 DN 131:286357
 ED Entered STN: 18 Aug 1999
 TI Design, Synthesis, and Activity of a Series of Pyrrolidine-3-carboxylic
 Acid-Based, Highly Specific, Orally Active ETB Antagonists Containing a
 Diphenylmethylamine Acetamide Side Chain
 AU Liu, Gang; Kozmina, Natasha S.; Winn, Martin; von
 Geldern, Thomas W.; Chiou, William J.; Dixon, Douglas B.; Nguyen,
 Bach; Marsh, Kennan C.; Oppenorth, Terry J.
 CS Metabolic Disease Research and Drug Analysis Department Pharmaceutical
 Products Division, Abbott Laboratories, Abbott Park,
 IL, 60064-6098, USA
 SO Journal of Medicinal Chemistry (1999), 42(18), 3679-3689
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1
 GI



AB The endothelin (ET)-B receptor subtype is expressed on vascular endothelial and smooth muscle cells and mediates both vasodilation and vasoconstriction. On the basis of the pharmacophore of the previously reported ETA-specific antagonist I (R1 = R2 = n-Bu; R3 = MeO) (ABT-627), we are reporting the discovery of a novel series of highly specific, orally active ETB receptor antagonists. Replacing the dibutylaminoacetamide group of I with a diphenylmethylaminoacetamide group resulted in antagonist I (R1 = (C6H5)2CH; R2 = H; R3 = MeO) with a complete reversal of receptor specificity. Structure-activity relationship studies revealed that ortho-alkylation of the Ph rings could further increase ETB affinity and also boost the ETA/ETB activity ratio of the resulting antagonists. A similar antagonism selectivity profile could also be achieved when one of the Ph rings of the acetamide side chain was replaced with an alkyl group, preferably a tert-Bu group I [R1 = C6H5(t-Bu)CH; R2 = H; R3 = MeO]. Combining these features with modification of the 2-aryl group of the pyrrolidine core, we have identified a potent antagonist I [R1 = (2-MeC6H4)2CH; R2 = H; R3 = MeOCH2CH2O] (A-308165) with over 27 000-fold selectivity favoring the ETB receptor and an acceptable pharmacokinetic

profile (F = 24%) in rats.

ST pyrrolidinecarboxylic acid prepn endothelin B antagonist; endothelin B antagonist structure activity relationship

IT Endothelin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ETA; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT Endothelin receptors
RL: SPN (Synthetic preparation); PREP (Preparation)
(ETB, antagonist; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT Endothelin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ETB; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT Structure-activity relationship
(endothelin receptor-binding; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT 246853-46-3P 246853-53-2P 246853-55-4P
246853-56-5P 246853-57-6P 246853-58-7P 246853-59-8P
246853-60-1P 246853-61-2P 246853-64-5P
246853-66-7P 246853-67-8P 246853-68-9P 246853-69-0P
246853-70-3P 246853-71-4P 246853-72-5P 246853-73-6P 246853-74-7P
246853-75-8P 246853-76-9P 246853-77-0P 246853-80-5P
246853-81-6P 246853-82-7P 246853-83-8P
246853-85-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT 246853-50-9P
RL: PUR (Purification or recovery); PREP (Preparation)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT 246853-51-0P
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT 100-09-4 1018-97-9, 2,2'-Dimethylbenzophenone 1485-00-3 27890-92-2
246853-48-5 246853-78-1 246853-79-2 246853-84-9 246853-86-1
246853-87-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT 2881-83-6P 173864-45-4P 173864-47-6P 218271-43-3P 246853-44-1P
246853-45-2P 246853-47-4P 246853-49-6P 246853-54-3P 246853-88-3P
246853-89-4P 246853-90-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

IT 108714-78-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, biol. activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

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- IT 246853-46-3P 246853-53-2P 246853-55-4P
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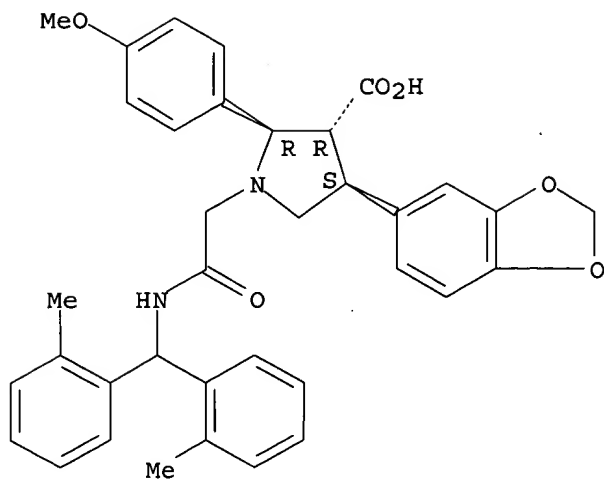
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

RN 246853-46-3 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

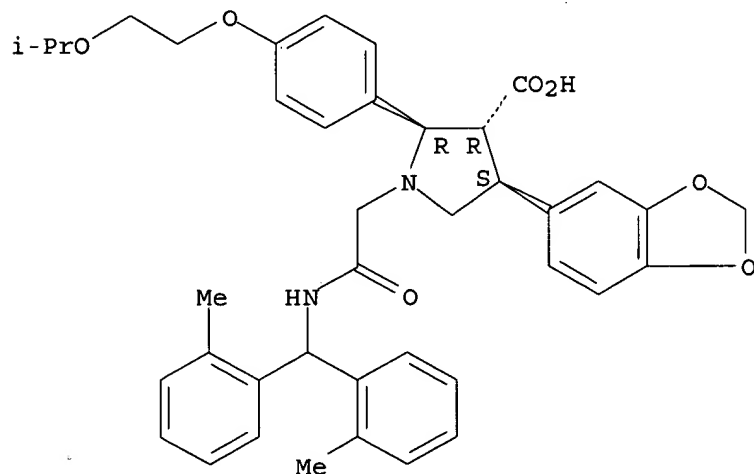
Relative stereochemistry.



RN 246853-53-2 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)

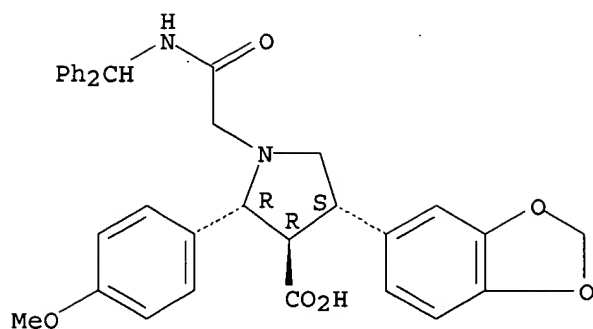
Absolute stereochemistry. Rotation (+).



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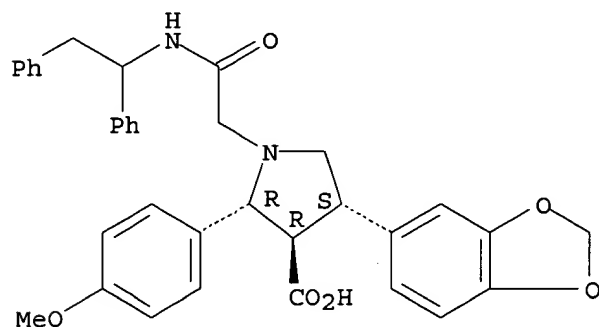
Relative stereochemistry.



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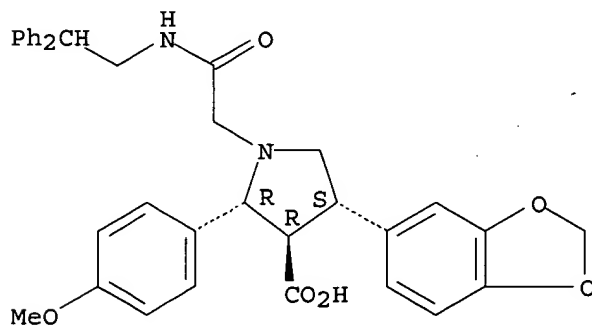
Relative stereochemistry.



RN 246853-58-7 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(2,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

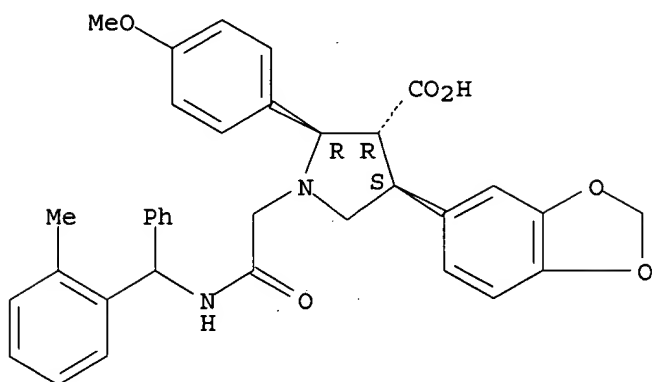


RN 246853-60-1 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-1-[2-[(2-methylphenyl)phenylmethyl]amino]-2-oxoethyl]-, (2R,3R,4S)-rel-

(9CI) (CA INDEX NAME)

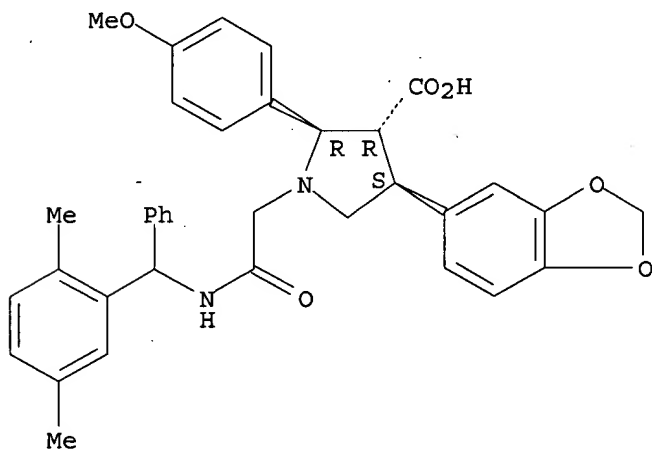
Relative stereochemistry.



RN 246853-61-2 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(2,5-dimethylphenyl)phenylmethyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 246853-64-5 HCAPLUS

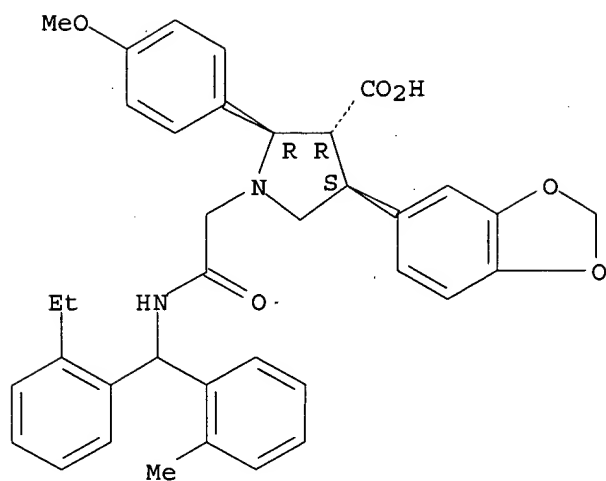
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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CRN 246853-63-4

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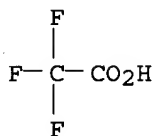
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 246853-66-7 HCAPLUS

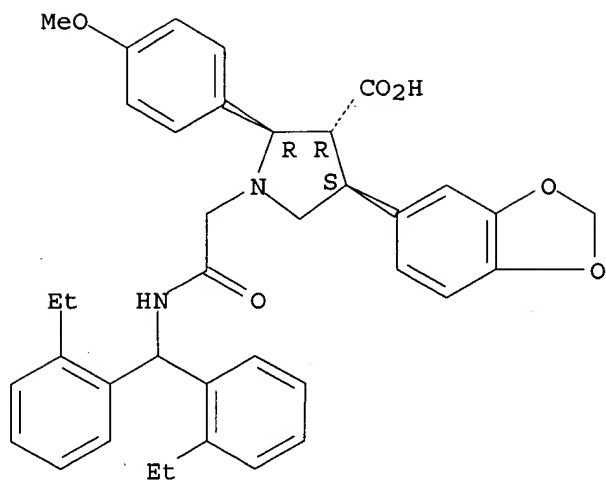
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-ethylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 246853-65-6

CMF C38 H40 N2 O6

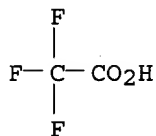
Relative stereochemistry.



CM 2

CRN 76-05-1

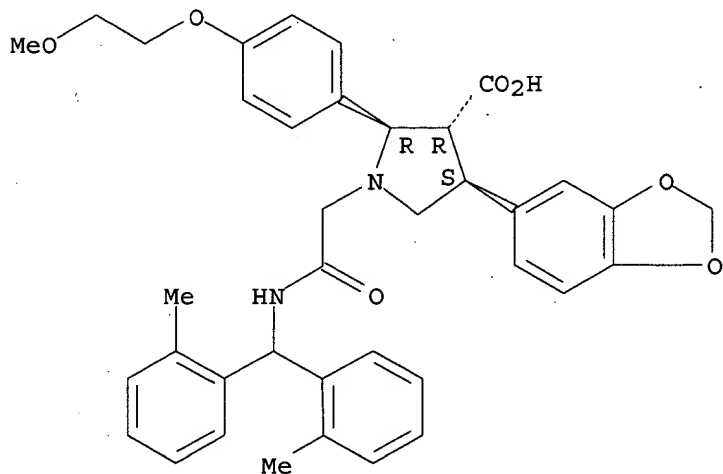
CMF C2 H F3 O2



RN 246853-81-6 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

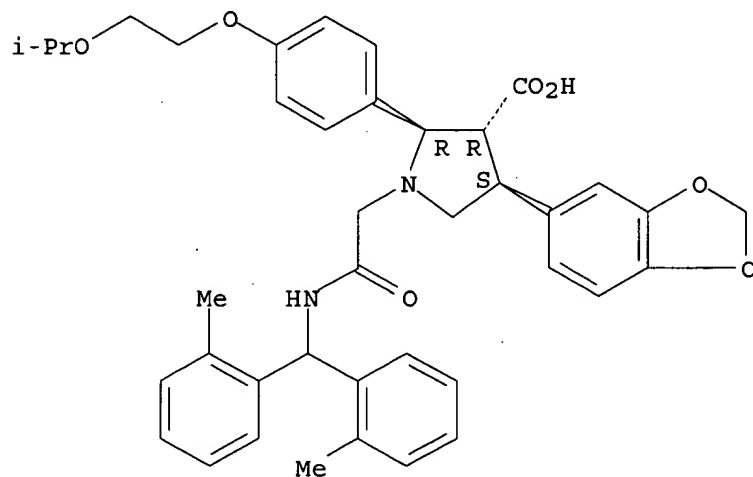
Relative stereochemistry.



RN 246853-82-7 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

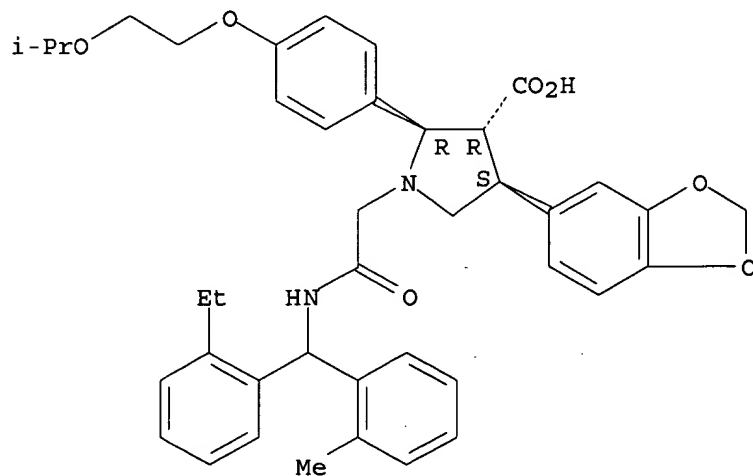
Relative stereochemistry.



RN 246853-83-8 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

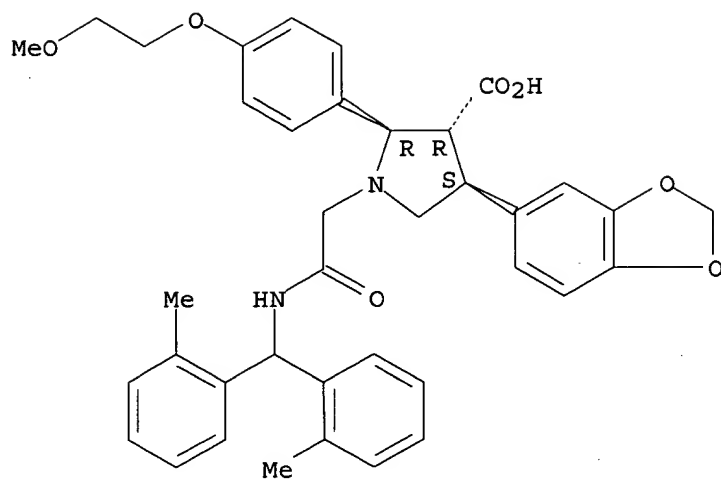
Relative stereochemistry.



RN 246853-85-0 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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SET COST OFF

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L2 0 S L1 CSS
L3 STR L1
L4 1 S L3
L5 STR L3
L6 38 S L5
L7 2808 S L5 FUL
SAV L7 SHIAO653/A

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L10 155 S E3-E9, E13
E BOYD S/AU
L11 101 S E3, E4
E BOYD STEVE/AU
L12 60 S E4, E5
E HUTCHINS C/AU
L13 70 S E3, E10, E13, E16, E17
E JAE H/AU
L14 43 S E5, E13, E14
E TASKER A/AU
L15 63 S E3, E8, E9
E ON GELDERN T/AU
E VON GELDERN T/AU
L16 92 S E3-E8
E VONGELDERN T/AU
L17 3 S E4
E GELDERN T/AU
L18 1 S E4
E KESTER J/AU

L19 25 S E3,E11-E14
 E SORENSEN B/AU
 L20 16 S E3,E8
 L21 40 S E46
 E SZCZEPANKIEWICZ B/AU
 L22 43 S E4-E7
 E HENRY K/AU
 E SZCZEPANKIEWICZ B/AU
 L23 1 S E2
 E HENRY K/AU
 L24 15 S E3,E7
 L25 34 S E35,E37-E39
 E LIU G/AU
 L26 843 S E3-E29
 E LIU GANG/AU
 L27 869 S LIU GANG?/AU
 E WITTENBERGER S/AU
 L28 61 S E4-E8
 E KING S/AU
 L29 54 S E3,E4
 E KING STEVE/AU
 L30 71 S E3,E4,E7-E9
 E JANUS T/AU
 L31 15 S E4,E6,E7
 E PADLEY R/AU
 L32 28 S E4-E6
 E ABBOT/PA,CS
 L33 147 S E3,E4
 E ABBOTT/PA,CS
 L34 8778 S E3,E4
 L35 197 S L7
 L36 1 S L9 AND L35
 L37 54 S L8-L34 AND L35
 L38 54 S L36,L37
 L39 0 S L38 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
 L40 6 S L35 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
 L41 10 S L35 AND (PY<=1995 AND PRY<=1995 OR AY<=1995)
 L42 3 S L38 AND L41
 L43 7 S L41 NOT L42
 L44 2 S L43 NOT 74/SC,SX
 L45 4 S L36,L42

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 L48 2273 S L7 AND L47

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L51 287 S L7 AND L50
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SAV L53 SHIAO653A/A

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S L55 AND L1-L34

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FILE 'HCAPLUS' ENTERED AT 15:38:44 ON 28 JUN 2005
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L64 2 S L63 AND L8-L34,L56-L58
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